## SECUENCE LISTING

1

1 .

Flint, Andrew J.

Cool, Dehorah E. AND IMPROVED ASSAY FOR PROTEIN TYROSINE : HESPHATES 200125.401 <1: 05/09/788,626 <111-2001-02-13 - 1 mg. 40 · PastSEQ for Windows Version 4.0 · 2 1 2 · · 1 · ; : : 11 · ; : : PRT -::: Artificial Sequence

...! · VARIANT (1)...(1)

... Xaa = Ile or Val

...3 VARIANT

(4)...(4)

... Xaa - any amino acid

... VAFIANT

\_... (7)...(7)

, } Xaa = any amino acid

.. 1 · VAFTANT

0.002 = (8)...(8)0.003 = 0.003 amino acid

TMAIHANT :

4.11. (10) ... (10)

· ( >> Xaa = Ser or Thr

0.022 imes 0 Unique signature sequence motif which is invariant among all PTPs.

100 - 1

cia His Cys Xaa Ala Gly Xaa Xaa Arg Xaa Gly

:210≥ 2

- 2117 254

-312× FPT

-01: Homo sapiens

< 400 - 2 Asp Phe Pro Cys Arg Val Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn 10 Arg Tyr Arg Asp Val Cer Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Glu 40 Ala Gln Arg Ser Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys 55 Gly His Phe Trp Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val 75 70 Met Leu Asn Arg Val Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr 90 85 Irp Pro Gln Lys Glu Glu Lys Glu Met Ile Phe Glu Asp Thr Asn Leu 1.05 1()() Lys Leu Thr Leu Ile Ser Glu Asp Ile Lys Ser Tyr Tyr Thr Val Leu 120 Glu Leu Glu Asn Leu Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe 140 135 His Tyr Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser 155 150 Phe Leu Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro 165 170 Glu His Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly Arg Ser 185 190 130 Gly Thr Phe Cys Leu Ala Asp Thr Cys Leu Leu Heu Met Asp Lys Arg 200 205 195 Lys Asp Pro Ser Ser Val Asp Ilo Lys Lys Val Leu Leu Glu Mot Arg 210 215 Lys Fhe Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser 230 235 Tyr Ieu Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp 245

<210> 3

<211> 251 <212> PRT

<213> Homo sapiens

< 100 × 3

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Ala Glu Asn Asp Tyr Ile Asn Ala Ser Leu Val Asp Ile Glu Glu Ala 35 40 45

Gln Arg Ser Tyr Ile Leu Thr Gln Gly Fro Leu Pro Asn Thr Cys Cys 50 60

His Phe Trp Leu Met Val Trp Gln Gln Lys Thr Lys Ala Val Val Met 65 76 80

Leu Asn Arg Ile Val Glu Lys Glu Ser Val Lys Cys Ala Gln Tyr Trp

Pro Thr Asp Asp Gin Glu Met Leu Phe Lys Glu Thr Gly Phe Cer Val 105 100 hys ben ben Ser Glu Asp Val Lys Ser Tyr Tyr Thr Val ben Gln ben 120 Glu Asn Ile Asn Ser Gly Glu Thr Arg Thr Ile Ser His Phe His Tyr 140 135 Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu 155 1.50 Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Asn Pro Asp His 165 Gly Pro Ala Val Ile His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr 190 180 185 Pho Ser Leu Val Asp Thr Cys Leu Val Leu Met Glu Lys Gly Asp Asp 195 200 205 lle Asn The Lys Gln Val Leu Leu Asn Met Arg Lys Tyr Arg Met Gly 215 Leu Ile Glo Thr Pro Asp Glo Leo Arg Phe Ser Tyr Met Ala Ile Ile 230 235 Glu Gly Ala Lys Cys Ilo Lys Gly Asp Ger Cer <210> 4 <211> 317 -212 PRT <213> Homō sapiens Gly lle Thr Ala Asp Ser Ser Asn His Pro Asp Asn Lys His Lys Asn 10 ] Arg Tyr lie Asn ile Val Ala Tyr Asp His Ser Arg Val Lys Leu Ala 30 Gln Leu Ala Glu Lys Asp Gly Lys Leu Thr Asp Tyr Ile Asn Ala Asn 40 Tyr Val Asp Gly Tyr Asn Arg Fro Lys Ala Tyr Ile Ala Ala Gln Gly 60 55 Pro Leu Lys Ser Thr Ala Glu Asp Phe Trp Arg Met Ile Trp Glu Eis 75 7.0 Asn Val Glu Val Ile Val Met lle Thr Asn Leu Val Glu Lys Gly Arg 90 85 Arg Lys Cys Asp Gln Tyr Trp Pro Pro Ala Asp Gly Ser Glu Glu Tyr 105 100 Gly Asn Fhe Leu Val Thr Gln Lys Ser Val Gln Val Leu Ala Tyr Tyr 120 125 Thr Val the Thr Leu Arg Asn Thr Lys Ile Lys Lys Gly Ser Gin Lys 135 140 Gly Arg Fro Ser Gly Arg Val Val Thr Gln Tyr His Tyr Thr Gln Trp 155 150 ire Asp Met Gly Val Pro Glu Tyr Ser Leu Pro Val Leu Thr Phe Val 170 165 Ard Dys Ala Ala Tyr Ala Lys Arg His Ala Val Gly Pro Val Val Val 190 185 His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Val Leu Asp

200 Jer Met Leu Gln Gln Ile Gln His Glu Gly Thr Val Asn Ile Fhe Gly

	21 G					z. 1 <sup>1</sup>					220 •		1 .	11-1 L	
25 E					230		(ilri			235					2.41)
ilu i	Gln	Tyr		1-1160	He	His	Asp	Thr	Leu 250	Val	Glu	Ala	Ile	Leu 255	Ser
ys '	Glu	Thi	Glu	245 Val	Val	Leni	Asp	Ser 265		Leu	Gln	Gln	Ile 270	Gln	His
Slu	Gly			Asn	11€	Fhe	Gly 280		Leu	Lys	His	Ile 285		Ser	Glr
		275 Tyr	Leu	Val	Gln	Thr 295	Glu	Glu	Ğln	Tyr			lle	His	Asp
Thr 305	290 Leu	Val	Glu				Ser	Lys	Glu			Val			
212	> 3 > Pl	5L	sapir	p <sub>1</sub> gr											
.400 31y	) · 5	Thr	Ala	Asp	Ser	Ser	Asn	His	Pro	Asp	Asn	Lys	His	Lys 15	Ası
l Arg	Tyr	Tle		5 He	Val	Ala	Tyr	Asp 25	10 His	Ser	Arg	Val	Lys 30		Al
51 m	Leu		20 G1u	Lys	Asp	Gly	Lys 40		Thr	Āsp	Tyr	11e 45		Ala	As
Tyr		35 Asp	Gly	Гуг	Asn	Arg	Pro	Lys	Ala	Tyr	I1e 60		Ala	Gln	Gl
	50 Leu	Lys	: Umr	Thr	Ala Vo		Asp	Phe	Trp	Arg	-	Ile	Trp	Glu	Hi 80
65 Asn	Val	Glu	. Val	114 85	Va1	Met	He	Thr	Asn 90		Val	Glu	Lys	Gly 95	Ar
Arg	Lys	Cys	Asp 100	Glr	Tyr	Trp	Pro	Ala 105	Asp	Gly	Ser	Glu	Glu 110	Tyr	Gl
Asn	Phe	Le:	ı Val	Thr	Gln	Lys	Ser 120	Val		Val	Leu	Ala 125	. Tyr	Tyr	Th
Val	Ph∈	Thi	Leu	Arg	Asn	Thr 135	Lys	Ile	Lys	Lys	Gly 140	Ser	Gln	Lys	Gl
Arg 145	Pro	Sei	Gly	Arg	Val 150	Val	Thr	Gln	Tyr	His 155	Tyr	Thr	: Gln	Trp	Pr 16
Asp				165	Glu	Tyr	- Ser		-170	)				1/5	,
			1 % (	Ala	Lys		g His	185	,				190	)	
		1 1	1 4117	∵ Vail			7hr 20(	1				205	)		
	. 14	1 -31:	1 1111			215	s Glu				2.20	)			
5-5-6	1.73	- H.i			2.31	1	n Ar			2.35	/				2 -
Plr				241	· His	s Asp	) Thr		250	)				45.	7
1	Т.	. 11	1 74		Tariji.	ı Asp	p 361	r Met	. Let		Glr	1116	e Glr 270	n His	s G.

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GIV Thr Val Ash Ilo Phe Gly the Lea bys His Ile Arg Ser Gln Arg
                      2.60
Asn Tyr beu Val Gin Thr Glu Glu Glu Tyr Val Phe He His Asp Thr
                                     300
             2.5%
bed Val Glu Ala Ile Leu Ser Lys Glu Thr Glu Val
                310
-210 > 6
2211> 319
-212> PRT
<213> Homo sapiens
<400 > 6
Ash Ile Thr Ala Glu His Ser Ash His Pro Glu Ash Lys His Lys Ash
                              1.0
          5
Arg Tyr He Asn Ile beu Ala Tyr Asp His Ser Arg Val Lys beu Arg
       ZÜ
Pro Lou Pro Gly Lys Asp Cer Lys His Jer Asp Tyr Ilo Asn Ala Asn
                       10
Tyr Val Asp Gly Tyr Asn bys Ala Lys Ala Tyr lle Ala Thr Gln Gly
                                  60
                    55
   50
Pro Leu Lys Ser Thr Phe Glu Asp Phe Trp Arg Met Ile Trp Glu Gln
                                 75
                 70
Asn Thr Gly lie lie Val Met lie Thr Asn beu Val Glu Lys Gly Arg
                               (11)
           8.5
Arg Lys Cys Asp Gln Tyr Trp Pro Thr Glu Asn Ser Glu Glu Tyr Gly
                                            110
                          105
          106
Asr. The the Wal Thr Leu Lys Ser Thr Lyc the His Ala Cys Tyr Thr
                               125
                       120
       115
Val Phe Ser lie Ard Ash Thr Lys Val Lys Gly Gln Lys Gly Ash
                     135
Pro Lys Gly Arg Gln Asn Glu Arg Val Val Ile Gln Tyr His Tyr Thr
          150
                                   155
 Gin Trp Pro Asp Met Gly Vai Pro Glu Tyr Ala Leu Pro Val Leu Thr
                              170 175
             165
 Phe Val Arg Arg Ser Ser Ala Ala Arg Met Pro Glu Thr Gly Pro Val
                           185
                                             190
           180
 Leu Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Val
                       200
  195
 lle Asp Ser Met Leu Gln Gln Ile Lys Asp Lys Ser Thr Val Asn Val
    210 214 220
 Leu Gly Phe Leu Lys His Il- Arg Thr Gln Arg Asn Tyr Leu Val Gln
                230 235
 Thr Glu Glu Gin Tyr lle the lle His Asp Ala Leu Leu Glu Ala Ile
              240 250 255
 ber Gly Lys Glo Thr Glo Val Vol He Asp Jer Met Leu Gln Gln He
        260 265 270
 Lys Asp Lys Ser Thr Val Ash Val Lou Sty Phys I on Lys His Ile Arg
275 286 286
 Thr Glm Aru Asm Tyr Leu Val Glm Thr Glm Glm Glm Tyr Ile Phe Ile
                2 4E)
                                      300
 His Asp Ala Lou Lou Glu Ala 110 Lou Gly Lys Glu Thr Glu Val
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\cdot 210 \cdot 7
+211 + 313
-212- PRT
213> Drosophila melanogaster
Asp Leu Pro Cys Glu His Ber Gln His Fro Glu Ash Lys Arg Lys Ash
                                               15
                              1.0
Arg Tyr Leu Asn Ilo Thr Ala Tyr Asp His Ser Arg Val His Leu His
                                           30
                          25
       20
Pro Thr Pro Gly Gln Lys Lys Asn Leu Asp Tyr Ile Asn Ala Asn Phe
                       40
 35
Ile Asp Gly Tyr Gln Lys Gly His Ala Phe Ile Gly Thr Gln Gly Pro
                                    60
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Lea Pro Asp Thr Phe Asp Cys Fhe Trp Arg Met Ile Trp Glu Gln Arg
                                 75
Val Ala Ile Ile Val Met Ile Thr Asn Leu Val Glu Arg Gly Arg Arg
Lys Cys Asp Met Tyr Trp Fro Lys Asp Sty Vat He Thr Tyr Wry Val
                           105
          100
Ile Gln Val Lys Leu Ile Glu Glu Glu Val Met Ser Thr Tyr Thr Val
      115 120 125
Leu Gln Ile Lys His Leu Lys Leu Lys Lys Lys Gln Cys Asn Thr
       135
Glu Lys Leu Val Tyr Gln Tyr His Tyr Thr Ash Trp Frc Asp His Gly
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Thr Pro Asp His Pro Leu Pro Val Leu Asn Phe Val Lys Lys Ser Ser
                           170
       165
Ala Ala Ash Pro Ala Glu Ala Gly Pro 11- Val Val His Dys Per Ala
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     180
                         180
Gly Val Gly Arg Thr Gly Thr Tyr Ile Val Leu Asp Ala Met Leu Lys
       195 200 205
Gln Ile Gln Gln Lys Asn Ile Val Asn Val Phe Gly Phe Leu Arg His
    210 215 220
lle Arg Ala Gln Arg Asn Phe Leu Val Gln Thr Glu Glu Gln Tyr Ile
                230 235
Phe Leu His Asp Ala Leu Val Glu Ala Ile Ala Ser Gly Glu Thr Asn
        245 250 255
Leu Val Leu Asp Ala Met Leu Lys Gln Ile Gln Gln Lys Asn Ile Val
                                            270
          260 265
Asn Val Phe Gly Phe Leu Arg His Ile Arg Ala Gln Arg Asn the Leu
           280 285
    275
Val Gln Thr Glu Glu Gln Tyr lle Phe Leu His Asp Ala heu Val Glu
              295
 Ala Ile Ala Ser Gly Glu Thr Asn Leu
                 3.10
22102 B
 4.211 - 306
 - 112 - PRT
213x Homo sapiens
 4400≥ €
 Sin The Thr Trp Siu Ash Non Ash Leu Siu Tal Ash bys Fr Dys Ash
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Arg T								2 · ·							
Ser I		112 m	Gly				21 1 1					7 /			
Asp G	Пу	Tyr													
Pro 9	ilu				7.63					1 2					
65 Ala T				0.5	Met.				911						
Cys A			100	Trp				1115							
Glri V		2 2 5					1 / 1 /	Glu				4 4 - 17			
Ala l		115 His	Lys	Ser	Gly	Ser 135	Ser	Glu	Lys	Arg	Glu 110	Leu	Arq	Glri	Flic
Gln	130 Phet	Met,	Ala	Trp	Pro	Asp	His	āly	Val	Pro 155	ř;] ų	Tyr	Pro	Thr	Pro 160
145 11e	ieu	Ala	Fhe	I.eu	150 Arg	Arg	Val	Lys	Ala 170	Cys	Ash	Pro	liesu	Asp 175	Ala
Ğly	Pro	Met		165 Val	His	Cys	Ser	Ala 185	Gly	Val	Gly	Arg	Thr 190	Gly	Cys
Ph⋅≥	Tle		180 Ile	Asp	Ala	Met	Leu 200	Glu	Ārg	Met	Lys	His 205	Glu	hys	Thr
Val	Asp	195 Ile	Tyr	Gly	His	Val	Thr	СУБ	: Met	Arg	Ser 220	Gln		Asn	Tyr
M∉t.	210 Val	Gln	Thr	Glu	Asp	215 Glr	o n Tyr	Vāl	. Phe	11e 235	His	Glu	Ala	1.eu	Leu 240
				Cys	230 Gly				ı Val	L Vai					Leu
								. Va.	zan L Asp					: Val	Thr
			0.0				л Туі	zos Met	1				Asp		n Tyr
		- m r	_			Lei	z81 u Lei	!			a Th:	c Cys			Thr
Glu	290 Val	)				29	5				300	)			
305															
<21 C21	0> 9 1> 3														
<21	2> I	PRT	sap	iens											
Ser		a Er													в Азп
			· ()					-	L Hi	s Je			-		u Gln
Thr	Il			y As	p Th	r As	sri 34 40	r As	т,	r Il	e As	n Gl 45	; As	n Ty	r Ile
Asp	G1 50		r Hi	s Ar	g Pr	ā As Se	sn Hi	s T;	ar Il	le Al	a Th	r 31	r: 11	y Fr	u Met

Gln Glu Thr 110 Tyr Asp Phe Trp Ard Med Val Trp His Glu Ash Thr 70 Ala Ser Ile Ile Met Val Thr Asn Len Val Glu Val Gly Arg Val Lys 90 85 Cys Cis Lys Tyr Trp Pro Asp Asp Thr Glu Ile Tyr Lys Asp tle Lys 105 100 Va. Thr Leu Ile Glu Thr Glu Leu Leu Ala Glu Tyr Val Ile Phe Ala 115 120 Va. Giu Lys Arg Gly Val His Glu lle Arg Glu Ile Arg Gln Phe His 135 Phe Thr Gly Trp Pro Asp His Gly Val Pro Tyr His Ala Thr Gly Leu 150 155 145 Lea Gly Phe Val Arg Gln Val Lys Ser Lys Ser Pro Pro Ser Ala Gly 170 165 Pro Leu Val Val His Cys Ser Ala Gly Ala Gly Arg Thr Gly Cys Phe 180 185 190 lle Val lle Asp Ile Met Leu Asp Met Ala Glu Arg Glu Gly Val Val 205 200 Asp lle Tyr Asn Cys Val Arg Glu Lou Arg Jer Arg Ar; Val Asn Wêr 210 215 220 Val Gln Thr Glu Glu Gln Tyr Val Phe Ile His Asp Ala Ile Leu Glu 235 240 230 Ala Cys Leu Cys Gly Asp Thr Ser Val Val Ile Asp Ile Met Leu Asp 245 250 255 Met Ala Glu Arg Glu Gly Val Val Asp lle Tyr Asn Cys Val Arg Glu 265 270 Leu Arg Ser Arg Arg Val Asn Met Val Gln Thr Glu Glu Gln Tyr Val 275 280 285 Phe Ile His Asp Ala Ile Leu Glu Ala Cys Leu Cys Gly Asp Thr Ser 295 Val 3(5 <: 10> 10 <..111 310 <.:12: PRT <!13> Homo sapiens <4001 10 Gin Ala Thr Cys Glu Ala Ala Ser Lys Glu Glu Asn Lys Glu Lys Asn 5 10 Arg Tyr Val Asn Ile Leu Pro Tyr Asp His Ser Arg Val His Leu Thr 25 20 Pro Val Glu Gly Val Pro Asp Ser Asp Tyr Ile Asn Ala Ser Phe Ile 4.6 40 Asn Gly Tyr Gln Glu Lys Asn Lys Phe Ile Ala Ala Gln Gly Fro Lys 60 5.5 Glu Glu Thr Val Asn Asp Phe Trp Arg Met Ile Trp Glu Gln Asn Thr 75 7.0 Ala Thr Ile Val Met Val Thr Asn Leu Lys Glu Arg Lys Glu Cys Lys 90 Cys Ala Gin Tyr Trp Pro Asp Gln Gly Cys Trp Thr Tyr Gly Asn Ile 110 105 100 Arg Val Ser Val Glu Asp Val Thr Val Leu Val Asp Tyr Thr Val Ehe

		115					120			_		125	1	D	I
	156		Gli			136					1 4 17				
11e	Thr	Gln	Phi	His !	Phe '	Thr	Ser	Trp	Pro	Asp 155	Fhe	Gly	Val	Pro	Phe 160
145 Thr	Pro	Il∈	Gly	146 t . :	Leu	Lys	Phe	Leu	Lys 170	Lys	Val	Lys	Λlа	Cys 175	Asn
Pro	Gln	Tyr	Ala 180	165 Gly 7	Ala	He	Val	Val 185		Cys	Ser	Ala	Gly 190	Val	Gly
Arg	Thr	Gly 195	Thr	Phe '	Vāl	Val	11e 200	Asp	Ala	Met	Leu	Asp 205	Met	Met	His
Thr		Arg	Lys	Val.	Asp	Val 215	Tyr	Gly	Phe	Val	Ser 220	Arg	Ile	Arg	Ala
	210 Arg	Cys	Gln	Met	Val 230	Gln	Thr	Asp	Met	Gln 235	Tyr	Val	Phe	Ile	Tyr 240
225 Gln	Ala	Leu	Leu	Glu 245	Hs	Туг	Leu	Tyr	Gly 250		Thr	Glu	Leu	Val 255	Ile
Asp	Ala	Met	Leu	Asp	Иet	Met	Ніз	Thr		Arg	Lys	Val	Asp 270	Val	Туг
Gly	Phë		260 Ser	Arg	He	Arg	Ala 280		Arg	Cys	Gln	Met 285	Val	Gln	Thr
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Tyr 305			Thr	Glu	Leu 310										
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	3 H	OMO	sāpi	ens											
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<40 Gln 1 Arg Gln Asp Gln 65 Ala Cys	3. H O. 1. Gly Tyr Let: Gly 50. Glt. Thr His	omo  Thr Thr Asr 35 Tyr Th: Grant Th	Phe Phe 20 Asn 20 Gly Lys Val Val 100 S Val	Glu 5 Ile Ile Glu Asn Met 85 Trp Glu	Leu Fro Lys Asp 70 Leu Fro	Pro Cys Asn 55 Phe Thr Asp	Asn Ser 40 Lys Trp Asn GIn Val	Asp 25 Asp Phe Arc Let 10: Val	10 His His Tyr He Ho His Tyr Cyr He He He H	Ser Ile Ala Val 75 Glu STrp UVal	Arg Asn Ala 60 Trp Arg Thr	Val Ala 45 Glu Glu Tyr Tyr 125	Ile 30 Ser Gly Gln Glu Glu 110 Thr	Tyr Pro Lys Glu 95 Asn	Ser Ile Lys Ser 80 Lys Ile
<40 Gln 1 Arg Gln Asp Gln 65 Ala Cys	3. H  O. 1  Gly  Tyr  Let:  50  Glt.  Thr  His:  Val:	omo  Thr Thr Asr 35 Tyr Th: Chi	Phe Phe 20 Asn 20 Gly Lys Val Val 100 S Val 5 Nal 5 Pro	Glu 5 Ile Ile Glu Asn Met 85 Trp Glu Glu	Leu Fro Lys Asp 70 Leu Fro Asp	Pro Cys Asn 55 Phe Thr Asp Cys	Asn Ser 40 Lys Trp Asn GIn 120 Asp	Asp 25 Asp Phe Arc Let 10: Val	10 His His Tyr He He Hot He Hot He Hot He Hot	Series Ile Ala Val 75 Glu STrr Val	Arg Asn Ala 60 Trp Arg Thr Ass Ala 54	Val Ala 45 Glu Glu D Glu Tyr 125 A Fre	Ile 30 Ser Gly Gln Glu 110 Thr	Tyr Pro Lys Glu 95 Asn	Ser Lys Ser 80 Lys Ile Fhe
<100 Gln 1 Arg Gln Asp Gln 65 Ala Cys Arg Cys	3. H Old 1. Gly Tyr Lett 50 Glt Thr Hist 130 Glt	omo  1 Thr Fro Asr 35 Tyr Th: Cy: Cy: Cy: Cy: Ch. Let	Phe Phe 20 Asn 20 Gly Lys Val Val 100 S Val 5 From His	Glu 5 Ile Ile Glu Asn Met 85 Trp Glu Gln Gln	Leu Pro Lys Asp 70 Leu Pro Asp Leu Thr	Pro Cys Asn 55 Phe Thr Asp Cys Fro 139 Ser	Asn Ser 40 Lys Trp Asn GIn 120 Asp Asp	Asp 25 Asp Phe Arc Let 105 Val	10 His His Tyr His OTyr Hot Grap Gyr Cyr Cyr Cyr D Asp	Series Series Alace Alac	Arg Asn Ala 60 Trp Arg Thr Asp 140 Gl:	Val Ala 45 Glu Glu Tyr 125 a Pro Va.	Ile 30 Ser Gly Gln Gln Glu Thr Arc	Tyr Pro Lys Glu 95 Asn Het	Ser Ile Lys Ser 80 Lys Ile

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Val His Ala Gly Pro Ile Val Val His Tys Ser Ala Gly Val Gly Arg
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          180
Thr Gly Thr Phe Ile Val Ile Asp Ala Met Met Ala Met Met His Ala
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              200
Glu Gln Lys Val Asp Val Phe Glu Phe Val Ser Arg Ile Arg Asn Gln
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                    215
Arg Fro Gln Met Val Gln Thr Asp Met Gln Tyr Thr Phe ile Tyr Gln
                         235
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Ala Leu Leu Glu Tyr Tyr Leu Tyr Gly Asp Thr Glu Leu Val Ile Asp
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Ala Met Met Ala Met Met His Ala Glu Gln Lys Vai Asp Val Phe Glu
       260 265
Phe Val Ser Arg lie Arg Asn Gln Arg Pro Gln Met Val Gln Thr Asp
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Gly Asp Thr Glu Leu
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Arg Tyr Val Asp Ile Leu Pro Tyr Asp Tyr Asn Arg Val Glu Leu Ser
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                            25
           2.0
Glu lie Asn Gly Asp Ala Cly Ser Thr Tyr lle Asn Ala Ser Tyr Ile
                                 4.5
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 Asp Gly Phe Lys Glu Pro Arg Lys Tyr Ile Ala Ala Gln Gly Pro Arg
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 Asp Glu Thr Val Asp Asp Phe Trp Arg Met Ile Trp Glu Gln Lys Ala
                                    75
                 70
 Thr Val Ile Val Met Val Thr Arg Cys Glu Glu Gly Asn Arg Asn Lys
                                90
              8.5
 Cys Ala Glu Tyr Trp Pro Ser Met Glu Glu Gly Thr Arg Ala Phe Lys
                                              110
                            105
       100
 Asp Ile Val Val Thr Ile Asn Asp His Lys Arg Cys Pro Asp Tyr Ile
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                        120
    115
 lle Leu Asn Val Ala His Lys Lys Glu Lys Ala Thr Gly Arg Glu Val
    130
                                       140
 Thr His Ile Gin Phe Thr Ser Trp Pro Asp His Gly Val Pro Glu Asp
 145 150 255
 Pro His Leu Leu Lou Lys Leu Arg Arg Arg Val Asn Ala Phe Ser Asn
                                170
                                                 175
        165
 Phe Phe Ser Gly Pro Ile Val Val His Cys Ser Ala Gly Val Gly Arg
                             185
           180
 Thr Gly Thr Tyr Ile Gly Ile Asp Ala Met Leu Glu Gly Leu Glu Ala
                                           205
                         200
 Glu Gly Lys Val Asp Val Tyr Gly Tyr Val Val Lys Leu Arg Arg Gln
                                    220
                     215
 Arg Cys Leu Met Val Gln Val Glu Ala Gln Tyr Ile Leu Ile His Gln
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4.7
-2101
277
15,000
-
577
27.72
27.0

235 230 7.2. Ala Leu Val Glu Tyr Asn Gln Phe Gly Glu Thr Glu Val Gly He Asp 250 Ala Met beu Giu Gly Leu Glu Ala Glu Gly Lys Val Asp Val Tyr Gly 270 260 265 Tyr Val Val bys ben Arg Arg Gln Arg Cys ben Met Val Gln Val Glu 280 285 Ala Gin Tyr ile Leu ile His Gin Ala Leu Val Glu Tyr Asn Gin Phe 290 295 Gly Glu Thr Glu Val 305 <210> 13 <2112 325 <212≥ PRT ≈213> Homo sapiers - 100% - 13 Lea Tyr Cer Ary Eye Gla Gly Gln Arg Gln Glu Asn Eys Asn Eys Asn 10 Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr Arg Val Val Leu His 2.5 Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr Ile Asn Ala Asn Ile 4.0 The Met Pro Giu Phe Glu Thr Lys Cys Asn Asn Ser Lys Pro Lys Lys 55 Ser Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn Thr Val Asn Asp Phe 7.5 Trp Arg Met Val Phe Gln Glu Asn Ser Arg Val Ile Val Met Thr Thr 90 Lys Glu Val Glu Arg Gly Lys Ser Lys Cys Val Lys Tyr Trp Pro Asp 110 105 100 Glu Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg Val Arg Asn Val Lys 120 125 🖽 Ser Ala Ala His Asp Tyr Thr Leu Leu Lys Leu Ser Lys Val Gly 130 135 140 Oln Gly Asn Thr Glu Arg Thr Val Trp Gln Tyr His Phe Arg Thr Trp 145 150 155 Pro Asp His Gly Val Pro Ser Asp Pro Gly Gly Val Leu Asp Phe Leu 165 170 175 Glu Glu Val His His Lys Gln Glu Ser Ile Met Asp Ala Gly Pro Val 185 180 Val Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Phe Ile Val 205 200 The Asp the Leu the Asp The The Arg Glu Lys Gly Val Asp Cys Asp 215 220 270 The Asp Val Fro Lys Thr Ile Glm Met Val Arg Ser Glm Arg Ser Gly 235 240 230 1944 Wal Bir Thr Glu Ala Gln Tyr Arg Phe Ile Tyr Met Ala Wal Gln 245 250 His Tyr Ile Glu Thr Leu Gln Arg Arg Ile Val Ile Asp Ile Leu Ile 266 Asy the the Ard Glu Lys Gly Val Asp Cys Asp The Asp Val Pro Lys 280

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The He Gin Met Val Ary Ser Siln Ary Ser Gly Met Val Gin Thr Glu
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-211 - 322
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Gly Ard Asp Ser Ash lie Fro Gly Ser Asp Tyr He Ash Ala Ash Tyr
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The Lys Asn Gir. Leu Leu Gly Fro Asp Glu Asn Ala Lys Thr Tyr Ile
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 Glm Lys Thr Ile Glm Met Val Arg Ala Glm Arg Ser Gly Met Val Glm
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 Glu Thr Thr Lys Lys Lys has led Val IIo Asp Met Leu Met Glu Asn IIe
           260 265 270
 Jer Thr Lys Gly ben Asp Tys Asp The Asp The Gln Lys Thr Ile Gln
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 Met Val Ard Ala lin Ard Ser Gly Met Val Jin Thr Glu Ala Gln Tyr
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                                      300
 Lys Phe lie Tyr Val Ais ilo Ala Gln Phe lle Glu Thr Thr Lys Lys
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+ 1 + 1

Lys Liu

115

+210 - 152211 - 319 212 · PPT 2213 Homo sapiens < 400 - 15 Asn Gin Ser Cys Asp lie Ala Leu Leu Pro Giu Asn Arg Gly Lys Asn 10 1 Arg Tyr Asn Asn Ile Leu Pro Tyr Asp Ala Th: Arg Val Lys Leu Ser 25 20 Asn Val Asp Asp Asp Pro Cys Ser Asp Tyr Ile Asn Ala Ser Tyr Ile 45 40 Pro Gly Asn Asn Phe Arg Arg Glu Tyr He Vai Thr Gln Gly Pro Leu 55 Pro Gly Thr Lyn Asp Asp Phe Trr Lys Met Val Trp Glu Gla Asn Val 70 His Ash 114 Val Met Val Thr Glin Tyr Val the byr dly Ard Val Lys 7911 Cys Asp His Tyr Trp Fro Ala Asp Gla Asp Cer Leu Tyr Tyr Gly Asp 105 110 100 heu lie Leu Gln Met Leu Ser Glu Ser Val Leu Pro Glu Trp Thr Ile 120 The Lys lie Cys Gly Glu Glu Gln beu Asp Ala His Arg ben lie Arg 140 135 130 His Phe His Tyr Thr Val Trp Pro Asp His Gly Val Pro Glu Thr Thr 150 Gin Ser beu lle Gin Phe Val Ard Thr Val Ard Asp Tyr ll≃ Asn Ard 165 Ser Pro Gly Ala Gly Pro Thr Val Val His Cys Ser Ala Gly Val Gly 185 180 Arg Thr Gly Thr Phe Ile Ala Leu Asp Arg Ile Leu Gln Gln Leu Asp 205 200 Ser Lys Asp Ser Val Asp Ile Tyr Gly Ala Val His Asp Leu Arg Leu 210 215 220 His Arg Val His Met Val Gln Thr Glu Cys Gln Tyr Val Tyr Leu His 230 225 Gln Cys Val Arg Asp Val Leu Arg Ala Arg Lys Leu Arg Ser Ala Leu 250 245 Asp Arg Ile Leu Gln Gln Leu Asp Ser bys Asp Ser Val Asp Ile Tyr 260 265 Gly Ala Val His Asp Lou Arg Leu His Arg Val His Met Val Gln Thr Z.H.\* 280 Glu Cys Gin Tyr Mal Tyr Leu His Glr Cys Val Ary App Val Leu Arg Ala Ang Lys Leu Ang Sor ⊀()<sup>L</sup>) +210 + 162211 · 309 -21X - ERT · 213 · Frosophila delanogaster

-400 - 16Asp Gln Pro Cys Thr Phe Ala Asp Leu Pro Cys Ash Arg Pro Lys Ash 10 [1] 1 Arg Phe Thr Asn Ile Leu Pro Tyr Asp His Ger Arg Phe Lys Leu Glr. Pro Val Asp Asp Glu Gly Ser Asp Tyr Il- Asn Ala Asn Tyr Val 40 Pro Gly His Asn Ser Pro Arg Glu Phe Ile Val Thr Gln Gly Pro Seu 95 His Ser Thr Arg Asp Asp Phe Trp Arg Met Cys Trp Glu Ser Asn Ser 7.0 Arg Ala Ile Val Met Leu Thr Arg Cys Phe Glu Lys Gly Arg Glu Lys 85 90 Cys Asp Gln Tyr Trp Pro Asn Asp Thr Val Pro Val Phe Tyr Gly Asp 110 100 Ile Lys Val Glm Ile Leu Asn Asp Ser His Tyr Ala Asp Trp Val Met 120 115 Phe Met Leu Cys Arg Gly Ser Glu Gln Arg IIe Leu Arg His Phe His 140 Fhe Thr Trp Pro Asp Phe Gly Val Fro Asn Pro Pro Gln Thr Lou 150 155 Val Arg Phe Val Arg Ala Phe Arg Asp Arg Ile Cys Ala Glu Gln Arg 165 170 Pro Ile Val Val His Cys Ser Ala Gly Val Gly Arg Ser Gly Thr Fhe 190 1.85 180 Ile Thr Leu Asp Arg Ile Leu Gln Gln 11e Asn Thr Ser Asp Tyr Val 200 195 Asp lle Phe Gly Ile Val Tyr Ala Met Arg Lys Glu Arg Val Trp Met 220 215 Val Glm Thr Glu Gin Glm Tyr Itr Cym Ilo His Glm Cys Ion ben Ala 225 - 230 - 235 - 240 Val Leu Glu Gly Lys Glu Asn Ile Vai Gly Pro Thr Leu Asp Arg Ile 250 255 245 Leu Gln Gln Ile Asn Thr Ser Asp Tyr Val Asp Ile Phe Gly Ile Val 260 265 Tvr Ala Met Arg Glu Lys Arg Val Trp Met Val Gln Thr Glu Gln Gln 285 275 280 Tyr Ile Cys Ile His Gln Cys Leu Leu Ala Val Leu Glu Gly Lys Glu 300 295 Asn Ile Val Gly Pro 305 <210> 17 111× 313 <212> PRT -213> Homo sapiens <400> 17 Ser Gln Sor Gln Met Val Ala Jer Ala Ser Glu Asn Ash Ala Lys Ash 1 Ard Tyr Arg Ash Val Leu Pro Tyr Asp Trp Ser Ard Val Era Lou Lys Fro Ile His Glu Slu Fro Gly Je: Asp Tyr Ile Asn Ala Jer Pha Met

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Fro dily Leu Trp Ser Pro Glin Glu Phe He Ala Thi Glin dly Fro Leu
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Pro Gin Thr Val Gly Asp Phe Trp Arg Leu Val Trp Glu Gln Gin Ger
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His Thr Leu Val Met Leu Thr Asn Cys Met Glu Ala Gly Arg Val Lys
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Cy: Glu His Tyr Trp Pro Leu Asp Ser Gln Pro Cys Thr His Gly His
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Lel Arg Val Thr Leu Val Gly Glu Glu Val Met Glu Asn Trp Thr Val
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Led Leu Leu Gen Val Glu Glu Gln Lys Thr Leu Ser Val Arg Gln
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Phe His Tyr Gln Ala Trp Pro Asp His Gly Val Pro Ser Ser Pro Asp
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The Leu Leu Ala Phe Trp Arg Met Leu Arg Gln Trp Leu Asp Gln Thr
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Met Glu Gly Gly Pro Pro Ile Val His Cys Ser Ala Gly Val Gly Arg
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The Gly The Lou fle Ala Leu Asp Val Lou Leu Ary Gla Leu Gin Jer
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Glu Gly Leu Gly Pro Phe Ser Phe Val Arg Lys Met Arg Glu Ser
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Arg Fro Leu Met Val Gln Thr Glu Ala Gln Tyr Val Phe Leu His Gln
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Cys Tle Cys Gly Ser Ser Asn Ser Gln Pro Arg Pro Gln Pro Arg Ala
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Leu Asp Val Leu Leu Arg Gln Leu Gln Ser Glu Gly Leu Leu Gly Pro
 260 265
Ph.e Ser Phe Val Arg Lys Met Arg Glu Ser Arg Fro Leu Met Val Gin
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 Pro Ile Val Ser Thr Val Val Asp Phe Trp Arg Net Val Trp Gln Glu
                               75
                 70
 Arg Thr Pro Ile Ile Val Met Ile Thr Ash Ile Glu Glu Met Ash Glu
                              90
             85
 Lys Cys Thr Glu Tyr Trp Pro Glu Glu Gln Val Vai His Asp Gly Val
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	120					135					140			Trp	
	Ser	Trp	Pro	Asp	Glrı	Lys	Thr	Pro	Asp	Arg 155	Ala	Pro	Pro	1,4911	heu 160
145			_	(2)	150	~1	C10	7) 1 = a	nd a		G n	Glu	Glv	Pro	
				165					1/0					1/2	
			190					185					100	Thr	
Cys	Phe	lle 195	Ala	Thr	Ser	Ile	Cys 200	Cys	Gln	Gln	Leu	Arg 205	Arg	Glu	Gly
Val		Asp	Tle	Leu	Lys	Thr	Thr	Cys	Gln	Leu	Arg 220	Gln	Asp	Arg	Glγ
4- 1	2.10	-1.	22.1	mb. v	Cin	215 Clu	C15	Tur	(41 m	Phe		His	His	Ala	Met
25.25.1					231					2.30					27.
Ser	Leu	Tyr	Ala	Th: 245	Ser	Ile	СУЗ	Cys	250 250	OH	Fi클리	Aig	Arg	431u 255	1. 1
175.1	Val.	Δen	116	Len	Lvs	Thr	Thr	Cys	Gln	Leu	Arg	Gln	Asp	Arg	$G1\gamma$
			260					- 265					2 / 1	Ala	
Gly	Met	11e 275		Thr	СУз	GLU	280	1 Y 1	GIII	111/-	V4 ±	285			
Ser	Leu 290	Tyr													
<21	0 > 1	9													
< 21	1 % 3	13													
±21 <21	1 > 3 2 > F	13 RT	phil	a me.	lan pç	gast	er								
<21 ₹21 <21	1 > 3 2 > F 3 > L	13 RT rosc	phil	a me.	lanpq	gast	er								
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<pre>&lt;21 &lt;21 &lt;40 Asp 1 Arg Val</pre>	1 × 3 2 × F 3 × L 0 × 1 Arç Tyr	13 RT Frosc .9 Thr Pro	Thr Asp 20 Gly	Lys 5 1le Leu	Asn Lys Gln	Ser Ala Thr	Asp Tyr Thr	Asp 25 Asp	Glr Tyr	n Thr	Arg Asr	Val Ala 45	Lys 30 Asn	Leu Phe	Val
<pre>&lt;21 &lt;21 &lt;40 Asp 1 Arg</pre>	1 × 3 2 × F 3 × L 0 × 1 Arç Tyr	13 RT Frosc .9 Thr Pro	Thr Asp 20 Gly	Lys 5 1le Leu	Asn Lys Gln	Ser Ala Thr	Asp Tyr Thr	Asp 25 Asp	Glr Tyr	n Thr	Arg Asr Ala	Val Ala 45	Lys 30 Asn	Leu	Ala Val
<pre><?1 <21 <40 Asp 1 Arg Val Ile</pre></pre>	19 3 2> F 3> L 0> 1 0 Arg Tyr Tle	13 PRT Prosc .9 Thr Pro Pro Asr 35 Y Tyr	Thr Asp 20 Gly Lys	Lys 5 Ile Leu Glu	Asn Lys Gln Arg	Ser Ala Thr Lys	Asp Tyr Thr 40 Lys	Asp 25 Asp Phe	Glr Glr Tyr	n Thr Ile Cys	Arg Asr Ala 60	Val Ala 45 Glr	Lys 30 Asn Gly	Leu Phe	Ala Val Met Leu
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<pre>&lt;21 &lt;21 &lt;40 Asp 1 Arg Val Ile Glu 65 Glu Cys</pre>	1	13 PRT Prosc 9 Thr 2 Pro 35 Y Typ Thr e Ile	Thr Asp 20 Gly Lys Lys Val	Lys 5 1le Leu Glu Asp 1le 85	Asn Lys Gln Arg Asp 70 Leu	Ser Ala Thr Lys 55 Phe Thr	Asp Tyr Thr 40 Lys Trk Asr	Asp 25 Asp Phe Arc Let Va 10	Glr  Tyr  He  Glu  Glu  Glu  Glu  90  He  5	Thr Tle Cys Tle 75 U Glu	Arge Asr Alas Alas 60 Trp Type The	Val Ala Ala Glr Glv Asi	Lys 30 A Asm Gly Glr Lys Glr 11(	Leu Phe Pro His Ala 95 Phe	Ala Val Met Leu 80 Lys Gly
<pre>&lt;21 &lt;21 &lt;40 Asp 1 Arg Val Ile Glu 65 Glu Cys</pre>	1	13 PRT Prosc .9 g Thr c Pro 35 y Tyr r Thr e Ile	Thr Asp 20 n Gly c Lys r Ile val s Tyr 100 u Val	Lys 5 1le Leu Glu Asp 1le 85	Asn Lys Gln Arg Asp 70 Leu	Ser Ala Thr Lys 55 Phe Thr	Asp Tyr Thr 40 Lys Trp Asr Lys	Asp 25 Asp Phe Arc Let 10 a Gl	Glr  Tyr  He  Glu  Glu  Glu  Glu  90  He  5	Thr Tle Cys Tle 75 U Glu	Arge Asr Alas Alas 60 Trp Type The	Val Ala 45 Glr Glr Asr Lys	Lys 30 A Asn Gly Glr Lys Glr 11( y Asp	Leu Phe Pro His Ala 95 Phe	Ala Val Met Leu 80 Lys
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<pre><?1 %21 <40 Asp 1 Arg Val Ile 65 Glu 65 Glu Cys Asp Glu Glu Glu Cys</pre></pre>	1  3  2  F  3  E  E  E  E  E  E  E  E  E  E  E  E	13 PRT Prosc .9 Final Prosc S5 Final Thirder Ref Lec Line	Thr Asp 20 Gly Lys Lys Val S Tyr 100 U Val 5	Lys 5 1le Leu Glu Asp 1le 85 Trp Lys Lys	Asn Lys Gln Arg Asp 70 Leu Pro Pro	Ser Ala Thr Lys 55 Phe Thr Glu Ala Asr	Asp Tyr Thr 40 bys Trp Asr Asr 15ys 120 120 15ys	Asp 25 Asp Arc Arc 10 Gl	Glr  Tyr  He  Glr  Met  Glu  Glu  Glu  Ar  As	n Thr c Ile c Cys t Ile 75 u Glu c Asp g Lya	Arge Asr S Ala 60 Try D The S Th	Value	Lys 30 A Asn Gly Glr Lys Glr 11( y Asp 5	Leu Phe Pro His Ala 95 Fhe D Tyr	Ala Val Met Leu 80 Lys Gly Ile Asp
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			180				Gly	185					1 11)		
		105	Arg				Leu 200					200			
	210	Glu				215	Val				220				
225	Arg				230	Fhe	Leu			235					2.40
Phe	Leu	Tyr	Arg	Ala 245	Lou	Leu	Asp	Thr	Gly 250	Thr	Phe	Gly	Asn	Thr 255	Asp
			260	Ser			Gln	265					2/0		
		275	Asn				Asp 280	Leu				250			
Val	Gln 290	Ser	L⊕J	Lys	Gln	Tyr 295	Ile	Phe	Leu	Туг	Arg 300	Ala	Leu	Leu	Asp
Thr 305		Thr	Phe	Gly	Asn 310	Thi	Asp	He							
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1				E-7			Leu		10				Lys	10	
			20					2.5					30		
		3 5					Thr					45			
	E ()					5.5	Ala -				Ćυ				
55					70		e Trp			75					80
				8.5					9C					90	Lys
			100	)				1.05					TTC	)	Gly
		170	5				120					172	)		Lys
	13-	)				-135	5				140				Thr
1 4 5					150	)				155					160
				16'	)				170	)				1/0	
			180	]				185	)				131	J	i Pro
		1 G	_				200	)				∠0:	)		c Phe
	2.17	1				21	5				42	J			e Leu
Ası	n Va	l Fh	e Gli	n Th	r Va.	l Se	r Ar	g Het	Arc	g Thi	Glr	Ar	g Al	a fhe	: 361

25715	
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41 1	

1. 20 230 60. He Gln Thr Pro Glu Gln Tyr Tyr Phe Cys Tyr Lys Ala He Leu Glu 21,0 2. t, t, 245 the Ala Ser Leu Asp Ile Cys Leu Ala Gln Leu Glu Glu Leu Gly Thr 265 260 Lou Ash Val The Gln Thr Val Ser Arg Mot Arg Thr Gln Arg Ala Phe 275 280 Ser Ile Gln Thr Pro Glu Gln Tyr Tyr Phe Cys Tyr Lys Ala fle Leu 300 295 Glu Phe Ala 305 <210> 21 ₹211 / 312 22122 FRT -2132 Homo sapiens · 400 - 21 The Ty: tro The Ala Thr Gly Glu Lys Glu Glu Ash Val Lys Lys Ash 10 F) Arg Tyr Lys Asp Ile Leu Pro Pho Asp His Ser Arg Val Lys Leu Thr 30 25 Leu Lys Thr Pro Ser Gln Asp Ser Asp Tyr Ile Asn Ala Asn Phe Ile 45 40 Lys Gly Val Tyr Gly Pro Lys Ala Tyr Val Ala Thr Gln Gly Pro Leu 55 Ala Asn Thr Val Ile Asp Phe Trp Arg Met Val Trp Glu Tyr Asn Val 75 7.0 Val lle Tie Val Met Ala Cys Arg Glu Phe Glu Met Gly Arg Lys 90 85 Cys Glu Arg Tyr Trp Pro Leu Tvr Gly Glu Asp Pro Ile Thr Phe Ala 100 105 110 Pro Phe Lys lle Ser Cys Glu Asp Glu Gln Ala Arg Thr Asp Tyr Phe 120 125 115 lie Leu Leu Leu Glu Phe Gln Asn Glu Ser Arg Arg Leu Tyr Gln Phe 140 135 His Tyr Val Asn Trp Pro Asp His Asp Val Fro Ser Ser Phe Asp Ser 145 150 155 lle Leu Asp Met Ile Ser Leu Met Arg Lys Tyr Gln Glu His Glu Asp 170 175 165 Val Pro the Cys Ile His Cys Ser Ala Gly Cys Gly Arg Thr Gly Ala 190 185 180 Ile Cys Ala Ile Asp Tyr Thr Trp Asn Leu Leu Lys Ala Gly Lys Ile 205 200 Pro Glu Glu The Asn Väl Phe Asn Leu Ile Gln Glu Met Arg Thr Gln 210 215 220 Arj His Ser Ala Val Gln Thr Lys Glu Gln Tyr Glu Leu Val His Arg 230 235 Ala II. Ala Gln Leu Phe Glu Lys Gln Leu Gln Leu Tyr Ala Ile Asp 255 250 245 Tyr Thr Trp Asn Leu Leu Lys Ala Gly Lys Ile Pro Glu Glu Phe Asn 260 265 270 Val The Asn Lou Ile Gln Glu Met Arg Thr Gln Arg His Ser Ala Val 280

Gir. Thr bys Glu Gln Tyr Glu Leu Val His Arg Ala ile Ala Gln Leu 295 the Glu Lys Gin bea Gln Leu Tyr 310 345 . 2111 - 22 -211 > 291 <212 PRT 22132 Homo sapiens ₹400> 22 Gly Leu Ala Ile Thr Phe Ala Lys Leu Pro Gln Asn Leu Asp Lys Asn 10 1 Arg Tyr Lys Asp Val Leu Pro Tyr Asp Thr Thr Arg Val Leu Leu Gln 30 25 20 Gly Asn Glu Asp Tyr Ile Asn Ala Ser Tyr Val Asn Met Glu Ile Pro 4.0 Ala Ala Ash ler War Ash Lys Tyr Ile Ala Thr Gln Gly Pro Leu Pro 60 5,4) His Thr Cys Ala Gin the Trp Gln Val Val Trp Asp Gln Lys Leu Ser 7.5 Leu Ile Val Met Leu Thr Thr Leu Thr Glu Arg Gly Arg Thr Lys Cys 90 85 His Gln Tyr Trp Pro Asp Pro Pro Asp Val Met Asn His Gly Gly Phe 105 110 100 His Ile Gln Cys Gln Ser Glu Asp Cys Thr Ile Ala Tyr Val Ser Met 115 120 125 Led Val Thr Ash Thr Gln Thr Gly Glu Glu His Thr Val Thr His Leu 140 135 Gin Tyr Val Ala Trp tro Asp His Gry Ile Pro Asp Asp Ser Ser Asp 155 150 Phe Leu Glu Phe Val Asn Tyr Val Arg Ser Leu Arg Val Asp Ser Glu 170 165 Pro Val Leu Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Val Leu 190 190 135 Val Thr Met Glu Thr Ala Met Cys Leu Thr Glu Arg Asn Leu Fro Ile 195 205 Tyr Pro Leu Asp ile Val Arg Lys Met Arg Asp Gln Arg Ala Met Met 215 220 Val Gln Thr Ser Ser Gln Tyr Lys Phe Val Cys Glu Ala Ile Leu Arg 230 235 240 Val Tyr Thr Het Glu Thr Ala Met Cys Leu Thr Glu Arg Asn Leu Pro 245 250 255 The Tyr has her Asp The Val Arg Lys Met Arg Asp Sin Arg Ala Met 265 270 2. 6,61 Met Val Glo The For Ger Glo Tyr Lys Phe Val Cys Glu Ala Ile Leu 285 2.90 .77 Ard Val Tyr 2. 114 · 2100 - 23 · 811 · 311 -111 - PRT

outs out by continuous dispositation

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4:01: 2.5
Pro Ner Glu Thr Der Glu Gly Asp Dys Lys Hip Ash Thr Ger Lys Ash
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Arg Tyr Thr Asn Ile Leu Pro Val Asn His Thr Arg Val Gln Leu Lys
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bys Ile Gln Asp byš Glu Gly Jer Asp Tyr Ile Ash Ala Ash Tyr Ile
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                       40
Asp Gly Ala Tyr Pro Lyn Gln Phe lle Cys Thr Gln Gly Pro Leu Pro
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The Lys Cys Asp Arg Tyr Trp Pro Glu Gln The Gly Gly Glu Gln Phe
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Ser lle Tyr Gly Ash Gly Ash Glu Val Fhe Gly Thr Tyr Ser Val Glu
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how Wall old Wal like dim tys Arg Old lis lie Thr Arg Ast. He Arg
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                                    140
beu Thr Fho Glu Gly Glu Thr Arg Asp Ile Thr Gin Tyr Gln Tyr Glu
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Gly Trp Pro Asp His Asn Tle Pro Asp His Thr Gln Pro Phe Arg Gln
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Leu Leu His Ser lie Thr Ash Ar; Gln Ash Gln He Fle Pro Ser Ser
                          185
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Asp Arg Asn Val Pro !le lle Val His Cys Ser Ala Gly Val Gly Arg
                              205
 195
The Gly The Phe Cys The Ala Val II) Met Met bys bys beu Asp His zlu $\rm 220
Tyr Phe Lys Glin Lou Asp Tyr Asr. Ser Arg Ile Asp Phe Asn Leu Phe
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Ser Ile Val Leu Lys beu Arg Glu Gin Arg Pro Gly Met Val Gln Gln
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Lou Glu Gln Tyr Leu Fhe Cys Tyr Lys Thr Ile Leu Asp Glu Ile Tyr
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His Arg Leu Asn Cys Thr Ala Val 11e Met Met Lys Lys Leu Asp His
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Tyr Phe Lys Gln Leu Asp Tyr Asn Ser Arg Ile Asp Phe Asn Leu Phe
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Ser Ile Vai Leu Lys Lou Arg Glu Sln Arg Pro Gly Met Val Gln Gln
           310
Leu Glu Gln Tyr Leu Phe Cys Tyr Lys Thr Ile Leu Asp Glu Ile Tyr
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 His Ard Leu Ash Cys
           +40
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· 210 · 24

F211- 312

<sup>· 2125</sup> FRI

<sup>·213.</sup> Schizosac are mycha pomka

e.400 - 24.

aim Try, Der Thr Wal Asy Jer Leu Jor Ash Thr Jet Tyr Lys Lys Ash

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Arg Tyr Thr Asp. Lie Val Pro Tyr Ash Cys Thr Arg Val His bou bys
      2.10
Arg Thr Ser Pro Ser Glu Leu Asp Tyr He Ach Ala Ser Phe He bys
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Thr Glu Thr Der Ash Tyr 114 Ala Cys Olf. Gly Der 11e Der Ard Der
              9.5
Ile Ser Asp Phe Trp His Met Val Trp Asp Asm Val Glu Asm ile Gly
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Thr Ile Val Met Leu Gly Ser Leu Phé Glu Ala Gly Arg Glu Met Cys
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             8.5
Thr Ala Tyr Trp Pro Ser Ash Gly Ile Gly Asp Lys Gln Val Tyr Gly
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Asp Tyr Cys Val Lys Gln Ile Ser Glu Glu Asn Val Asp Asn Ser Arg
                                         125
           120
      115
Phe He Leu Phe Glu He Gln Ash Ala Ash Phe Pro Ser Val Lys Lys
   130 13%
Val His His Tyr Gln Tyr Pro Ash Trp Ser Asp Cys Ash Ser Fre Glu
145 105 105
Asn Val Lys Sor Met Val Glu Fhe Leu Lys Tyr Val Asn Aen Cer His
        165
Gly Ser Gly Asn Thr The Val His Cys Ser Ala Gly Val Gly Ard Thr
180 185 190
Gly Thr Pho Ile Val Leu Asp Thr Ile Leu Arg Phe Pro Glu Ser Lys
             200
       195
Leu Ser Gly Phe Asn Pro Ser Val Ala Asp Ser Ser Asp Val Val Phe
                         220
   210 215
Gin Leu Val Asp His lie Arg Lys Gln Arg Met Lys Met Val Gin Thr
                     the Thr Sln Phe Lys Tyr Val Tyr Asp Lea 11e Asp Ner Lea Val Lea
245 250 250
Asp Thr Ile Leu Arg Phe Pro Glu Ser Lys Leu Ser Gly Phe Asn Pro
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Gly Ash Lys Lys Tyr lie Ala Cys Gin Ala Fre Lys fre Gly The Leu

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		115					120					125			
	Phi-	Thr		Arg I		Thir 135	Lys				140				
1 4 5	Fro			Arg '	/al ' 150	Val				155					1 0 0
				Pro (	Glu '				170					1 "	
			Tyr	Ala				180					7 7 7		
		105	Gly	Val (			200					ZUJ			
	210	Gln		Ile		215					220				
0:5	Lys			Arg	Ser 230	Gln				2.30					2. 19.12
Gin				11e	His				-250					6 11	
			1. 563	Val				1.6					1.		
		075	Asn	lle			-280					400			
Asn	Tyr 290	Leu	Val	Gln	Thr	Glu 295	Glu	Gln	Tyr	Val	Phe 300	Ile	His	Asp	Thr
Leu 305	Val	Glu	Ala	Ile	Leu 310	Ser	Lys	Glu	Thr	Glu 315	Val				
$\leq 21$	0≥ 2 1 ≥ 2														
<.31	2 × P 3 × H	RT omo													
<.31 <40 Thr	2  P 3  H 0  2 Ser	RT omo 7 Arg	Phe	Ile					1 U					10	Asn
<.21 <40 Thr 1 Arg	2 P 3 H 0 > 2 Ser Leu	RT omo 7 Arg Val	Phe Asn	Ile 5 Ile	Met	Pro	Tyr	Glu 25	Leu Leu	Thr	Arg	Val	. Cys 30	Leu	Gln
<40 Thr 1 Arg	2 P 3 H 0 > 2 Ser Leu	RT omo 7 Arg Val e Arg	Phe Asn 20 Gly	Ile 5 Ile Val	Met Glu	Pro Gly	Tyr Ser	Glu 25 Asp	Leu Tyr	Thr	Arg Asr	Val Ala 45	Cys 30 Ser	Leu Phe	Gln Leu
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<21 <40 Thr 1 Arg Fro Asp	2  P 3  H 0 > 2 Ser Leu Tle Gly 50 Glu	RT OMO 7 Arg Val Arg 35 7 Tyr	Phe Asn 20 Gly Arg	Ile 5 Ile Val Gln	Met Glu Gln Asp	Pro Gly Lys 55 Phe	Tyr Ser 40 Ala	Glu 25 Asp Tyr Arg	Leu Tyr Ile	Thr Ile Ala Let 75	Arg Asr Thr 60	Val Ala 45 Glr	Cys 30 Ser Gly His	Leu Phe Pro	Gln Leu Leu Ser 80
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<pre>&lt;31 &lt;40 Thr 1 Arg Fro Asp Ala 65 Thr Cys</pre>	2  P	RT OMO 7 Arg Val Arg 35 Tyr Ser E Ile	Phe Asn 20 Gly Arg Thr Val	Ile 5 Ile Val Glu Met 85 Trp Met	Met Glu Gln Asp 70 Leu Pro	Pro Gly Lys 55 Phe Thr	Tyr Ser 40 Ala Trp Lys Glu 1791	Glu 25 Asp Tyr Arc Arc 105 Asr	Leu Leu Tyr Ile Met Arc 90 Ger	Thr Ile Ala Let 75 Glu Ala Pro	Arge Asr A Thr 60 Trr Met	Vala Ala 45 Glr Glr Glr Ty 12	Cys 30 30 30 30 31 31 41 41 51 51 61 61 61 61 61 61 61 61 61 61 61 61 61	Leu Phe Pro Asn Glu G5 Tyr Leu	Gln Leu Ser 80 Lys The
<pre>&lt;21 &lt;40 Thr 1 Arg Pro Asp Ala 65 Thr Cys Val Lys</pre>	2 P P 3 P H S P P P P P P P P P P P P P P P P P	RT OMO 7 Arg Val Arg 35 Tyr Ser Glr 1 Asr 115	Phe Asn 20 Gly Arg Thr Val Tyr 100 Pro	Ile 5 Ile 5 Ile Val Glu Glu Met 85 Trp Met Ala	Met Glu Gln Asp 70 Leu Pro Ala Arg	Pro Gly Lys 55 Pho Thr Ala Gli (Asp	Tyr Ser 40 Ala Trp Lys Glu 120 Glu	Glu 25 Asp Tyr Arc Leu 105 Asi ()	Leu Leu Tyr Ile	Thr Ile Ala Let 75 Glu Ala Pro	Arge Asra Thr 60 Trp Met Arc Glr Thr 140	Ala 45 Glr Glr Gly Ty 12 12 11:	Cys 30 30 30 Ser Gly His Y Arg 110 The Arg	Leu Phe Pro Asn Glu 95 Tyr beu	Gln Leu Ser 80 Lys The Pher
<pre>&lt;21 &lt;40 Thr 1 Arg Fro Asp Ala 65 Thr Cys Val Lyo Gli 1</pre>	2 P P 3 H H O S 2 P P P P P P P P P P P P P P P P P P	RT OMO 7 Arg Val Arg 35 Tyr Ser Glr Asp 115 115 1 Thi 0 e Thi	Phe Asn 20 Gly Arg Thr Val 100 Fro Asp	Ile 5 Ile 5 Ile Val Glu Glu Met 85 Trp Met Ala	Met Glu Gln Asp 70 Leu Pro Ala Arg	Pro Gly Lys 55 Phe Thr Ala Gli Asr 13'	Tyr  Ser  40  Ala  Trp  Lys  Glu  120  Gli  Gli  Gli  Gli  Gli	Glu 25 Asp Tyr Arc Leu Arc 105 Asr Glu Glu	Leu Leu Tyr Ile Met Arç 90 Ge: Met Met Ne:	Thr Ile Ala Let 75 Glu Ala Pro As	Arge Asra Thr 60 Trp Met Arc Glr Th 140 Clr 55	Ala Ala Ab Glr Glr Ty 12 Th	Cys 30 30 Ser Gly His Arg THE Arg Cor Glr Cor Glr Cor Glr	Leu Phe Pro Asn Glu 95 Tyr Leu Glr Glr Glr	Gln Leu Ser 80 Lys The

Glm Asp Gly Pro 11e Thr Val His Cys Der Ala Gly Val Gly Arg Thr 185 180 Gly Val Phe Ile Thr Leu Ser Ile Val ben Glu Arg Met Arg Tyr Glu 200 195 Gly Val Val Asp Met Phe Gln Thr Val Lys Thr Leu Arg Thr Gln Arg 220 215 Pro Ala Met Val Gln Thr Glu Asp Gln Tyr Gln Leu Cys Tyr Arg Ala 235 230 Al. Leu Glu Tyr Leu Thr Leu Ser Ile Val Leu Glu Arg Met Arg Tyr 250 245 Glu Gly Val Val Asp Met Phe Gln Thr Val Lys Thr Leu Arg Thr Gln 260 265 Ary Pro Ala Met Val Gln Thr Glu Asp Gln Tyr Gln Leu Cys Tyr Arg 280 Ala Ala Leu Glu Tyr Leu 290 <210> 28 4211 4 281 <212> PRT <213> Homo sapiens <400> 28 Asn Asp Lys Met Arg Thr Gly Asn Leu Pro Ala Asn Met Lys Lys Asn Arg Val Leu Gln Ile Ile Pro Tyr Glu Phe Asn Arg Val Ile Ile Pro 25 20 Val Lys Arg Gly Glu Asn Asp Lys Met Arg Thr Gly Asn Leu Pro Ala 4 () Ash Mot Lys Lys Ash Arg Val Len Gln lle lle Pro Tyr Glo Phe Ash 5.5 Arg Val Ile Ile Pro Val Lys Arg Gly Glu Glu Asn Thr Asp Tyr Val 75 70

Asn Ala Ser Phe Ile Asp Gly Tyr Arg Gln Lys Asp Ser Tyr Ile Ala 90 Ser Gln Gly Pro Leu Leu His Thr Ile Glu Asp Phe Trp Arg Met Ile 100 105 Tip Glu Trp Lys Ser Cys Ser Ile Val Met Leu Thr Giu Leu Glu Glu 120 125 115 Arg Gly Gln Glu Lys Cys Ala Gln Tyr Trp Pro Ser Asp Gly Leu Val 140 135 Ser Tyr Gly Asp Ile Thr Val Glu Leu Lys Lys Glu Glu Glu Cys Glu 155 150 Ser Tyr Thr Val Leu Leu Val Thr Asn Thr Arg Glu Asn Lys Ser Arg 165 170 Gin Ile Arg Gln Phe His Fhe His Gly Trp Pro Glu Val Gly Ile Fro 185 180 Ser Asp Gly Lys Gly Met Ile Ser Ile Ile Ala Ala Val Gin Lys Gln 2015 200 195 G.n Gln Gln Ser Gly Asn His Pro Ile Thr Val His Cys Ser Ala Gly 215 220 Ala Gly Arg Thr Gly Thr Fhe Cys Ala Leu Ser Thr Val Leu Glu Arg 235 230 Val Lys Ala Glu Gly Ile Leu Asp Val Phe Gln Thr Val Lys Ser Leu

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Cys Tyr Lys Val Val Gin Giu Tyr Ile
+210× 29
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<212× PRT
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Met Lys Arg Gly Gln Glu Tyr Thr Asp Tyr lle Asn Ala Ser Phe Ile
                      40
Asp Gl; Tyr Arg Cin Lys Asp Tyr the Tle Ala Thr Gln Gly Pro Leu
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Ala His Thr Val Glu Asp Phe Trp Arg Met Ile Trp Glu Trp Lys Ser
               70
                                75
His Thr Ile Val Met Leu Thr Glu Val Glr Glu Arg Glu Gln Asp Lys
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Cys Tyr Gln Tyr Trp Fro Thr Glu Gly Ser Val Thr His Gly Glu Ile
  100 105 110
Thr Ile Glu Ile Lys Asn Asp Thr Leu Ser Glu Ala Ile Ser Ile Phe
 115 120
                                     125
leu Val Thr Leu Asn Gln Pro Gln Ala Arg Gln Glu Glu Gln Val Arg
   130 135 140
Val Val Arg Gln Phe His Phe His Gly Trp Pro Glu lle Gly Ile Pro
                150 155
Ala Glu Gly Lys Gly Met Ile Asp Leu Ile Ala Ala Val Gln Lys Gln
                   170 175
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Gln Gln Gln Thr Gly Asn His Pro Ile Thr Val His Cys Ser Ala Gly
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Ala Gly Arg Thr Gly Thr Phe Ile Ala Leu Ser Asn Ile Leu Glu Arg
             200 205
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 Val Lys Ala Glu Gly Leu Leu Asp Val Phe Gln Ala Val Lys Ser Leu
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 Arg Leu Gln Arg Pro His Met Val Gln Thr Leu Glu Gln Tyr Glu Phe
                               235
 225 230
 Cys Tyr Lys Val Val Gln Asp Phe Ile Ala Leu Ser Asn Ile Leu Glu
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 Arg Val Lys Ala Glu Gly Leu Leu Asp Val Phc Gln Ala Val Lys Ser
          260 265 270
 Leu Arg Leu Gln Arg Pro His Met Val Gln Thr Leu Glu Gln Tyr Glu
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                 280
       275
 Phe Cys Tyr Lys Val Val Gln Asp Phe Ile
                    295
 3210> 30
 ≥211 - 301
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10

Arj Ash Jer Ash Val Val Pro Tyr Asp Phe Ash Arg Val Pro Leu Lys 20 25 30 His He beu Glu Met Ser Lys Glu Ser Glu Pro Glu Ser Asp Glu Ser 40 45

ther Asp. Asp. Asp. Ser. Asp. Ser. Glu. Glu. Thr. Ser. Lys. Tyr. He. Asn. Ala r, ( ) Der Phe Val Met Der Tyr Trp Lys Pro Glu Met Met He Ala Ala Gln 75 70 Gly Pro Leu Lys Glu Thr Ile Gly Asp Phe Trp Gln Met Ile Phe Gln 9/1 Arg Lys Val Lys Val 11c Val Met Leu Thr Glu heu Val Asn Gly Asp 105 110 100 Glm Glu Val Cys Ala Glm Tyr Trp Gly Glu Gly Lys Glm Thr Tyr Gly 125 120 115 Asp Met Glu Val Glu Met Lys Asp Thr Asn Arg Ala Ser Ala Tyr Thr 140 135 Leu Phe Glu Leu Arg His Ser Lys Arg Lys Glu Pro Arg Thr Val Tyr 155 150 Gln Tyr Gln Cys Thr Thr Trp Lys Gly Glu Glu Leu Pro Ala Glu Pro 175 166 Lys Asp Leu Val Ber Met lie Gin Asp Leu Lys Gin Lys Leu Pro Lys 185 Ala Jor Fro His Gly Mar By: Tyr Hiz Lys His Ala Ser Ile Leu Val 2 (11) His Cys Arg Asp Gly Ser Gln Gln Thr Gly Leu Phe Cys Ala Leu Phe 220 215 Asn Leu Leu Glu Ser Ala Glu Thr Glu Asp Val Val Asp Val Phe Gln 240 230 235 Val Val Lys Ser Lou Arg Lys Ala Arg Pro Sty Val Val Cys Ser Tyr 255 250 245 Glu Gln Tyr Gln Phe Leu Tyr Asp Ile Iie Ala Ser Ile Tyr Pro Ala 265 260 Gin Asn Gly Gin Vai Ala Lou Fhe Asn Leu Leu Glu Ser Ala Glu Thr 285 Glu Asp Val Val Asp Vai Phe Gin Val Val Lys Ser Leu Arg Lys Ala 295 300 290 Arg Pro Gly Val Val Cys Ser Tyr Glu Gln Tyr Gln Phe Leu Tyr Asp 310 315 305 He He Ala Ser The Tyr Pro Ala Gin Asn Gly Gin Val 330 325

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<211> 295

<212> PRT

< 400 → 32

\*213> Drosophila melaneguster

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The The Lew Unit Hot life For this file thy Aspedly Fro Arg Lys Cys

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Pro Arg Tyr Trp Ala Asp Asp Glu Val Glu Tyr Asp His He hou Val
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         1(.)
                       11:19
Lys Tyr Val His Cer Clu Cer Cys Fro Tyr Tyr Thr Pho Pho Tyr Val
                              125
                       120
The Asn Cys Lys lie Asp Asp The Leu Lys Val The Gle Phe Gle Tyr
                                    140
                135
Asn Gly Trp Fro Thr Val Asp Gly Glu Val Fro Glu Val Cys Arg Gly
                                155
145
lle lle Glu Leu Val Asp Gln Ala Tyr Asn His Tyr Lys Asn Asn Lys
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      165
Asn Ser Gly Cys Arg Ser Fro Leu Thr Val His Cys Ser Leu Gly Thr
                                           130
   180
Asp Arg Ser Ser Ile Phe Val Ala Mot Cys Ile Leu Val Gln His Leu
 190 200
Arg Leu Glu Lys Cys Val Asp TIe Cys Ala Thr Thr Arg Lys Leu Arg \times 10 220
Ser Gin Ard Thr Gly Leu ile Ash Jer Tyr Ald Gin Tyr Glu Phe beu
His Ang Ala Ile Ile Ash fyr Ala Med Cys Ile Leu Val Gla His Leu
            245 250 255
Arg Leu Glu Lys Cys Val Asp IIn Cys Ala Thr Thr Arg Lys Leu Arg
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His Arg Ala Ile Ile Asn Tyr
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· 211x 30%
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Gln Ser Asp Tyr Ser Ala Ala Leu Lys Gln Cys Asn Arg Glu Lys Asn
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 Arg Thr Ser Ser Ile Ile Pro Val Glu Arg Ser Arg Val Gly Ile Ser
                                      30
                          25
        20
 Ser Leu Ser Gly Glu Gly Thr Asp Tyr Ile Asn Ala Ser Tyr Ile Met
                               45
           40
 Oly Tyr Tyr Gin Ser Ash Giu Pho lie lie Thr Gin His Pro Leu Leu
                           60
 50 55
 His Thr Ile Lys Asp Phe Trp Ara Met Ile Trp Asp His Asn Ala Gln
 ben Val Val Met lie fra Aspolly üln Asn Met Ala Gin Asp Glu Phe
                  **(*)
             H 47
 Val Tyr Trp Fro Asn Lys Asp Glu Fro Ile Asn Cys Glu Ger Phe bys
100 110
 Val Thr Leu Met Ala thu Glo His Lys Cys is a Jer Ash (Bu Glu Lys
       110 120
 Leu Ilê (le Fhq Ile Leu Glu Ala Thr Gin Asp Asp Tyr Vel Lêu Glu
130 - 125 - 149
 Val Arg His Pho Bin Cys Ito Lys Trp fro Ast Fro Asp Jor Ero He
145
```

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Ser Lys The Phe Glu Leu Ile Ser Vai Ile Lys Glu Glu Ala Ara Asa
            16,
Arg Asp Gly Pro Met Ile Val His Art Glu His Gly Gly Val Thr Aba
189 196
Gly Thr Phe Cys Ala Leu Thr Thr Leu Met His Gin Leu Glu Lys Glu
                            205
     195 200
Asn Ser Val Asp Val Tyr Gin Val Alâ Lys Met ile Asn Leu Met Arg
         215 220
Pro Gly Val Phe Ala Asp Ile Glu Gln Tyr Gln Phe Leu Tyr Lys Val
                      2.35
                                                240
          230
Lie Leu Ser Leu Val Ser Thr Arg Gln Glu Glu Asn Ala Leu Thr Thr
                   250 255
          245
beu Met His Gln Leu Glu Lys Glu Asn Ser Val Asp Val Tyr Gln Val
                                270
 260 265
Ala Lys Met Ile Asn Leu Met Arg Pro Gly Val Fhe Ala Asp Ile Glu
                                 285
 275 280
Gin Tyr Gln Phe Leu Tyr Lys Val Ile Leu Ser Leu Val Ser Thr Arg
   290
                  295
olm Glu old Ash
32105 34
<211> 308
<212> PRT
<213> Homo sapiens
<400> 34
Val Glu Cys Phe Ser Ala Gin Lys Glu Cys Asn bys Glu bys Asn Arg
Asn Ser Ser Val Val Pro for Glu Ary Ala Ard Val Gly Law Ala Fro
                          25
leu Pro Gly Met Lys Gly Thr Asp Tyr Ile Asn Ala Jer Tyr Ile Met
                      4 ()
      35
Cly Tyr Tyr Arg Ser Asn Glu Phe Ile Ile Thr Gln His Pro Leu Pro
                          60
                   55
    50
His Thr Thr Lys Asp Phe Trp Arg Met lle Trp Asp His Asn Ala Gln
                                 75
                7.0
Ile Ile Val Met Leu Pro Asp Asn Gln Ser Leu Ala Glu Asp Glu The
                          90
        85
Val Tyr Trp Pro Ser Arg Glu Glu Ser Met Asn Cys Glu Ala Phe Thr
       100 105 110
 Val Thr Leu Ile Ser Lys Asp Arg Leu Cys Leu Ser Asn Glu Glu Gln
                      120
    115
 lle Ile Ile Phe Ile Leu Glu Ala Thr Gln Asp Asp Tyr Val Leu Glu
                                   1.40
 130
 Val Arg His Phe Glm Cys Fro Lys Trp Fro Ash Fro Asp Ala Fro Ile
 145
                                 155
 Ser Ser Thr Phe Glu Leu Ile Asm Val Ile Lys Glu Glu Ala Leu Thr
            165
 Arg Asp Gly Pro Thr Ile Val His Asp Gin Tyr Gly Ala Val Der Ala
          180 185 190
 Gly Met Leu Cys Ala Leu Thr Thr Leu Cer Glin Glin Leu Glin Ash Glin
195 205
       195
 Ash Alo Val Asp Val Pho Eln Val Alo Dys Met Ile Ash bed Wet Arg
```

294) 27 ) 28 )

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214
  210
Fro Gly Val Phe Thr Asp 11e Glu Gln Tyr Gln Phe 11e Tyr Lys Ala
                  236
     230
Met Leu Ser Leu Val Ser Thr Lys Glu Asn Gly Asn Aig Leu Thr Thr
        245 250
beu Ser Gln Gln Leu Glu Asn Glu Asn Ala Val Asp Val The Gln Val
 260 265
Ala Lys Met Ile Asn Leu Met Arg Pro Gly Val Phe Thr Asp Ile Glu
 275 280 265
Gln Tyr Gln Phe Ile Tyr Lys Ala Met Leu Ser Leu Val Ser Thr Lys
290 295
Glu Asn Gly Asn
305
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~213> Drosophilä melanogaster
<400> 35
Glu Thr Asn Leu Met Ala Glu Gln Val Glu Glu Leu Lys Asn Cys Thr
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Pro Tyr Leu Glu Gln Gln Tyr Lys Asn Ile Ile Gln Phe Gln Pro Lys
 2.0
Asp Ile His Ile Ala Ser Ala Met Lys Gln Val Ash Ser Ile Lys Ash
                                   45
                    4.0
Arg Gly Ala Ile Phe Pro Ile Glu Gly Ser Arg Val His heu Thr Pro
                  5.5
Lys Pro Gly Glu Asp Gly Ser Asp Tyr Hle Ash Ala Fer Trp Leu His
                              7 5
65 70
Gly Phe Arg Arg Leu Arg Asp Phe Ile Val Thr Gln His Pro Met Ala
      85 90
His Thr Ile Lys Asp Phe Trp Gln Met Val Trp Asp His Asn Ala Gln
                       105
         100
Thr Val Val Leu Leu Ser Ser Leu Asp Asp Ile Asn Phe Ala Gln Phe
                     120
                                   125
Trp Pro Asp Glu Ala Thr Pro Ile Glu Ser Asp His Tyr Arg Val Lys
  130
                                 140
Phe Leu Asn Lys Thr Asn Lys Ser Asp Tyr Val Ser Phe Val Ile Gln
145 150 155
Ser Ile Gln Asp Asp Tyr Glu Leu Thr Val Lys Mot Leu His Cys Pro
                          170 175
            165
Ser Trp Pro Glu Met Ser Asn Pro Asn Ser Ile Tyr Asp Phe Ile Val
    180 185 190
 Asp Val His Glu Arg Cys Asn Asp Tyr Arg Asn Gly Pro Ile Val He
   195 200
                                   205
 Val Asp Arg Tyr Gly Gly Ala Gln Ala Cys Thr the Cys Ala Ile Ser
   210 215 226
 Ser Leu Ala Ile Glu Met Glu Tyr Cys Ser Thr Ala Ash Vai Tyr Gln
         230 23%
 Tyr Ala Lys Leu Tyr His Asn Lys Arg Pro Gly Val Trp Thr Ser Ser
                                        2 D D
           245 250
 Glu Asp Ile Arg Val Ile Tyr Asn Ile Leu Ser Fho Lou Fro Gly Asn
                26%
```

heu Asn hen heu bys Arg Ala Ile Cer der Leu Ala Ile Glo Met Glo 285 280 Tyr Cys Ser Thr Ala Asn Val Tyr Gln Tyr Ala Lys Leu Tyr His Asn 300 295 Lys Arg Pro Gly Val Trp Thr Ser Ser Glu Asp Ile Arg Val Ile Tyr 310 315 Asr. Ile Leu Ser Phe Leu Pro Gly Asn Leu Asn Leu Leu Lys Arg 330 < .. 10 > 35 <.111> 237 <.112> PRT <213> Yersinia sp. <400> 36 Thr Ash Asp Pro Arg Tyr Leu Gln Ala Cys Gly Glu Lys He Leu 10 Asn Arg Phe Arg Asp Ile Gln Cys Cys Arg Gln Thr Ala Val Arg Ala Asp Asn Tyr lle Gln Val Gly Asn Thr Arg Thr Ile Ala Cys Gln Tyr 40 Pro Leu Gln Ser Cln Leu Glu Ser His Phe Arg Met Leu Ala Glu Asn 5.5 60 Arg Thr Pro Val Leu Ala Val Leu Ala Ser Ser Ser Glu Ile Ala Asn 75 70 Gln Arg Phe Gly Met Pro Asp Tyr Phe Arg Gln Ser Gly Thr Tyr Gly 90 8.5 Ser Ile Thr Val Glu Ser Lys Met Thr Gln Gln Val Gly Leu Gly Asp 105 100 ely lld Asn Met Tyr Thr Leo Thr lle Arg Glu Ala Gly Gln Lys Thr 115 lle Ser Val Pro Yal Val His Val Gly Asn Trp Pro Asp Gln Thr Ala 135 Val Ser Ser Glu Val Thr Lys Ala Leu Ala Ser Leu Val Asp Gln Thr 145 150 155 Ala Glu Thr Lys Arg Asn Met Tyr Glu Ser Lys Gly Ser Ser Ala Val 165 Ala Asr Asp Ser Lys Leu Arg Pro Val lle His Cys Arg Ala Gly Val 180 185 190 Gly Arg Thr Ala Gln Leu Ile Gly Ala Met Cys Met Asn Asp Ser Arg 195 200 205 Asn Ser Gln Leu Ser Val Glu Asp Met Val Ser Gln Met Arg Val Gln 210 215 Arg Asn Gly Met Val Gln Lys Asp Glu Gln Leu Asp Val Leu Ile Lys 235 230 235 beu Ala Glu Gly Ala Met Cys Met Asn Asp Ser Arg Asn Ser Gln Leu 245 250 255 Ger Val Glu Asp Met Val Ser Gln Met Arg Val Gln Arg Asn Gly Mct

260 265 270

Val Gln Lys Asp Glu Gln Leu Asp Val Leu Ile Lys Leu Ala Giu 275 280 285

<2102 37 <211 7

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-212- PRT
13. Artificial Cequence
< 2300
< 233 Fluorescently-labeled phosphopeptides derived from
      amino acids 1170-1176 of the EGF receptor
      sequence.
KERLY PHOSPHORYLATION
< (4)...(4)
< 1.0 \cdot 37
Asn Ala Glu Tyr Leu Arg Val
<210 > 38
· 11 - 6
< dis PRI
3.x12 - Artificial Jequen 😁
< [ 2]10
<.23> Preferred substrate for PTB1B, corresponding to
      residues 988-993 of human EGF receptor.
<.21: PHOSPHORYLATION</pre>
< .22 > (5) ... (5)
+ 1100 38
h p Ala Asp Glu Tyr Leu
-110:39
 ...11: 11
 PRT
 111 Artificial Sequence
 :.? Substrate for PTBs synthesized from residues
       1142-1152 of human insulin receptor.
 3.1 - PROSPHORYLATION
 (£)...(5)
 C1 10> 39
 The Arg Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg
  . 10> 40
 1.11> 10
 <:12> PRT
 <213> Artificial Sequence
 PAZE Substrate for PTBs synthesized from residues
```

Con-509 of p561ck, the arc-like lymphocyte specific protein tyrosine kinase that is a physiological substrate for CD45.

· 221 · FHOSPHORYLATION

×222 · (6) . . . (6)

-400 - 40

Ala Thr Glu Gly Gin Tyr Gln Pro Gln Pro